THE GOOD DRUGS DO
new therapeutic waiting room supplement dedicated to the physician-patient relationship

Trib 45

Medical Tribune

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and Medical News

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From Heart Institute:

SIDS Linked to Familial Defect In QT Interval

Medical Tribune Report

ANAHEIM, CALIF.—A significant number of sudden and unexpected infant deaths may be linked to a familial cardiac mechanism characterized by a prolonged QT interval, a National Heart and Lung Institute team reported here.

Detailing the findings in a study that sought to shed light on the baffling problem of the sudden infant death syndrome (SIDS), the team told the American Heart Association that a "considerable proportion" of the first degree relatives of such infants have a prolonged QT interval on ECG examination.

Of 42 pairs of parents who were studied, prolongation of the interval was present in at least one parent in 11 pairs, or 26%. In addition, the prolonged QT interval was identified "in as many as 40% of the siblings" in these 11 families, suggesting an autosomal dominant pattern of inheritance, according to Dr. Barry J. Maron, of the Cardiology Branch, NHLI.

Underscoring the role of the QT abnormality in SIDS, Dr. Maron described the first known documentation of potential sudden death in an infant. The case was that of a "near-miss"

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Sputum Cytology: An Aid to Early Detection of Lung Ca

Medical Tribune Report

ANAHEIM, CALIF.—In patients in whom chest X-rays have failed to detect lung cancer, sputum cytology is becoming increasingly effective in the early detection and subsequent localization and treatment of the disease according to Dr. David R. Sanderson, Associate Professor of Medicine at the Mayo Medical School in Rochester, Minn.

The patients involved in his study had entered the Mayo Lung Project, part of an NCI-sponsored early lung cancer screening program involving men who are more than 45 years old and who smoke at least one pack of cigarettes a day, Dr. Sanderson told the 41st Annual Scientific Assembly of the American College of Chest Physicians. Each man who enters the program gives a complete health history, receives chest X-rays and submits sputum samples at four month intervals.

If the chest X-rays are negative, but the sputum cytology test indicates lung cancer cells, the search for the hidden tumor includes a detailed bronchoscopic evaluation of the patient under general anesthesia with collection of multiple samples from all parts of the bronchial tree for cytologic and histologic studies, Dr. Sanderson said. The search also includes a detailed study of

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Dr. Scribner Urges

Greater Use Of Dialysis At Home

Medical Tribune Report

NEW YORK—Stronger support from physicians for the use of home dialysis by suitable patients was urged here by Dr. Belding H. Scribner, developer of the arteriovenous shunt that bears his name and head of the Division of Nephrology at the University of Washington School of Medicine.

Dr. Scribner said that the proportion of patients with end-stage renal disease who are on home dialysis has declined over the past six years to the point where they now make up only 20% nationwide of all dialysis patients.

The drop began with the payment of dialysis costs under Medicare and the subsequent founding and expansion of large commercial dialysis centers, Dr. Scribner said at the annual meeting of the National Kidney Foundation, where he received the David M. Hume Memorial Award for his contributions to hemodialysis research.

Tracing specific causes, the Seattle specialist cited "lack of commitment and understanding on the part of physicians and staff" as the major reason for what he called the failure of home dialysis programs.

"If you are not fully committed to home dialysis, it's a lot harder to sell the patient on this form of care than to let him stay in centers and develop a

Continued on page 17

making rounds — at press time

MEDICAID EARNINGS - The publishing of names and addresses of 215 doctors who made $100,000 or more in 1974 for treating low-income patients carries "no implication of wrongdoing," an HEW spokesman told MT. "We have no way of knowing how large a doctor's overhead cost was," he added. However, HEW wants states to examine validity of claims. There has been no official response from the medical community so far, "but I'm sure there was some reaction. The publishing of the list resulted from a 'Freedom of Information' request from CBS," the spokesman said. "Under federal law, we are required to supply this information under most circumstances,"

Amputation Avoided in Osteogenic Sarcoma

By NATHAN HORWITZ
Medical Tribune Staff

NEW YORK—A new femoral prosthesis that makes it possible to avoid total leg amputation in selected patients with osteogenic sarcoma has been developed by a surgical team at Memorial Hospital-Sloan-Kettering Institute.

The vitallium device has been implanted in 18 pre-teen and teen-age patients and is functioning well in 14 at up to two years follow-up, according to Dr. Ralph C. Marcove, Acting Chief of the Bone Service at Memorial.

The patients can walk and move about easily with the aid of a cane, and some youngsters are able to walk up to four miles daily, Dr. Marcove told a symposium on "New Concepts in Treatment of Cancer" at Jewish Hospital and Medical Center of Brooklyn.

In conventional therapy, amputation is performed when an osteogenic sarcoma occurs at the head of the femur or along its length. However, recent advances in the chemotherapy of these tumors, Dr. Marcove noted, have significantly increased the survival rate of patients, creating the need to devise methods of limb salvage where possible.

Primary Indication

In Dr. Marcove's procedure, the primary indication for surgery is the localization of the sarcoma away from the neurovascular bundle of the leg. If the bundle can be completely freed by block resection through a margin of healthy tissue, the operation is performed, the surgeon said. The procedure entails en bloc removal of the knee joint and the entire femur, including the femoral part of the hip joint. Implantation of the prosthesis follows.

The patients continue receiving high dose combined therapy, in varying schedules, postoperatively. The drugs

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Vitallium femoral prosthesis is implanted in osteogenic sarcoma patient after removal of knee joint and femur, including femoral part of the hip joint.

Implant Avoids Amputation In Osteogenic Sarcoma

Continued from page 1

include vincristine, cytoxin, adriamycin and methotrexate with citrovorum factor rescue.

Of the 18 implants during the two-year trial, four have had to be removed: the causes were two cases of infection, one skin necrosis and one tumor recurrence.

Dr. Marcove reported that he and his team perform the operation even after metastatic spread of the tumor, provided the spread can be controlled for a useful period of time. "We have performed the procedure in two cases where pulmonary metastases had occured, when we were satisfied that control could be achieved," he reported.

Commenting on the trial in an interview, he said: "The fact is that initially we didn't think the prosthetic approach was possible in this disease, but we have found it is. Our first patient was a male who refused an amputation so that, perforce, we found ourselves trying the prosthesis. When we found that it worked, we continued the trials."

Dr. Michael Arlen, Physician-in-Chief of Neoplastic Surgery at Brooklyn Jewish Hospital, called Dr. Marcove's approach "among the most innovative operative procedures of the last decade in the treatment of this disease."

Photo of Dr. Marcove's prosthesis shows femoral head, shaft, hinged knee joint and tibial stem. At right, 17-year-old patient two years postoperatively. The girl is apparently free of disease and walks easily with aid of cane. Device has been implanted in 18 patients.

SIDS Linked to Familial Heart Defect

Continued from page 1

SIDS in a seven-week-old girl who was resuscitated after suffering sudden cardiorespiratory arrest. ECG studies in this infant showed "marked prolongation of the QT interval", Dr. Maron related.

"There was no clinical evidence of heart disease, and the patient was not given medications known to prolong the interval," he said. Although the child's parents had normal QT intervals, a prolongation of the QT interval was present in a 10-month-old nephew of the patient.

Data Suggestive

In an extension of the overall studies, Dr. Maron said, the team analyzed histologic sections of myocardium from 45 SIDS infants and 26 control infants. "Small foci of normal-sized, disorganized cardiac muscle cells were present in the ventricular septum of 22% of infants with SIDS and 12% of control infants," he reported. "The foci of disorganized cells in SIDS resembled those of symmetric septal hypertrophy (ASH) but were less marked in severity. Although the significance of these abnormally arranged cells is unknown, they may serve as a nidus for ventricular arrhythmias in some infants with SIDS," he declared.

Five sets of parents of infants with disorganized cardiac muscle cells were studied. Here, again suggesting the possibility of a familial link, "both ASH and prolonged QT intervals were present in a member of three of these five parental sets," Dr. Maron related.

In discussing these findings, Dr. Maron and his collaborators stressed that the data were necessarily suggestive, not conclusive. Prolonged QT interval syndrome is a known inheritable condition that is associated with cardiac arrhythmias, syncopic spells and sudden death.

What the NIH group has identified is a "relatively mild prolongation of the QT interval," Dr. Maron emphasized, adding that "the only definitive link to SIDS would be data obtained from SIDS infants during life." However, such infants are invariably considered healthy prior to their deaths. "In this regard, our finding of a marked prolongation of the QT interval is an infant with 'near miss' SIDS," Dr. Maron noted, "is confirmatory data of an association between SIDS and prolonged QT interval syndrome in some infants."

If the abnormality does play a role in SIDS, Dr. Maron said, it may operate in one of several ways: as a primary mechanism producing ventricular arrhythmia; or by creating a susceptibility to ventricular arrhythmia that is triggered by some environmental factor, such as infection; or as a secondary manifestation of a primary CNS abnormality.

"Although our results are not definitive," Dr. Maron concluded, "they do suggest that cardiac mechanisms, in particular those related to prolonged QT interval syndrome, are causally related to a substantial number of sudden and unexplained infant deaths."

Coauthors were Drs. Chester E. Clark, Robert E. Goldstein, Russell S. Fisher and Stephen E. Epstein.

Improved Access to Legal Abortion Drops N.Y.C. Pregnancy Rate

Medical Tribune Report

NEW YORK—Improved access to legal abortion appears to be associated with improved and more widespread use of contraceptive, according to an analysis of abortions, births and pregnancies among female residents of New York City since abortion was legalized here in 1970.

An increase of 14% in the rate of legal abortions between 1971 and 1973 was accompanied by a decrease of 7% in the rate of pregnancies, suggesting "more general and/or more effective practice" of contraception over the three-year period, reported Dr. Christopher Tietze, senior consultant with the Population Council.

The decline in pregnancies, Dr. Tietze found, was substantial for all age groups except teenagers, among whom the drop was "minimal."

New X-Ray Film

Medical Tribune Report

MADISON, WIS.—A new x-ray film and screen that significantly reduce patient exposure during mammography were demonstrated by the Eastman Kodak Company at the Mid-American Breast Cancer Symposium here. The new high-speed Min-R film and screen combination is reported to require approximately 34 times less exposure than films previously employed by radiologists for mammography.

index

CLINICAL NEWS NOTE: *"When there's a choice, chronic illness is always better treated at home than in an institution. The more responsibility the patient has for his welfare, the better the result. And the more informed the patient is about details of [home dialysis] treatment, and about complications and how to avoid them, the better the adjustment."* (Dr. Belding H. Scribner, University of Washington School of Medicine, Seattle. See page 1.)

feature index

On Page 9

A special section for your patients, edited by Dr. Louis Lasagna, which will help you build effective doctor-patient relationships by explaining

THE GOOD DRUGS DO

Put these pages, specially designed to be removed from Medical Tribune, in your waiting room.

Medical Tribune

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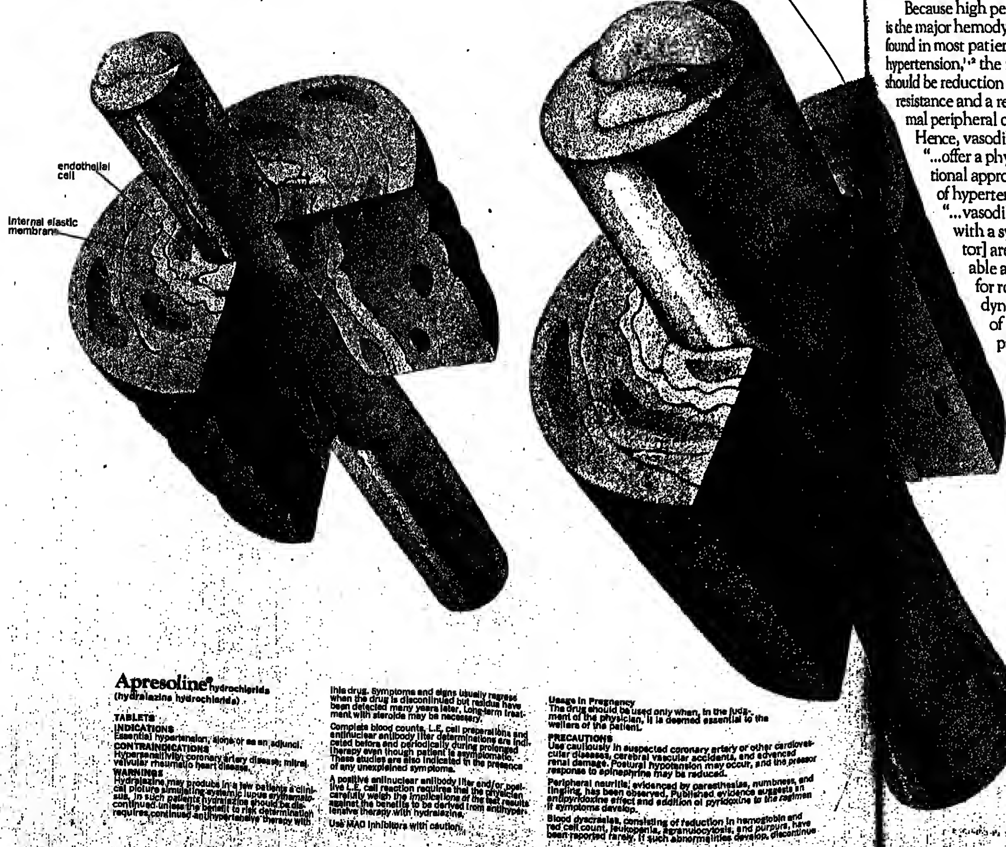

high peripheral resistance: common attribute of most hypertensives

Because high peripheral resistance is the major hemodynamic disturbance found in most patients with essential hypertension,[1,2] the therapeutic goal should be reduction of total peripheral resistance and a return to more normal peripheral circulation.[1,2]

Hence, vasodilating drugs "...offer a physiologically rational approach to the therapy of hypertension."[1] In addition, "...vasodilators [combined with a sympathetic inhibitor] are the most predictable and specific drugs for reversing the hemodynamic abnormality of most hypertensive patients."[3]

the only oral agent that deals directly with this problem

Apresoline (hydralazine), the only currently approved oral antihypertensive with vasodilating action, decreases peripheral resistance—regardless of its cause—and, hence, arterial pressure by relaxing arteriolar smooth muscle. Accompanying the fall in blood pressure is a rise in cardiac output and rate. Apresoline also maintains or increases renal and cerebral blood flow.

a different and complementary pharmacologic approach

Different in action from all other oral antihypertensives and compatible with most of them, Apresoline can play a significant role in a variety of therapeutic combinations.

Such combinations, according to Freis,[4] with each component representing a different antihypertensive mechanism, provide the most effective way to control blood pressure. This approach may also permit lower drug dosages.

the problem of postural hypotension minimized

Nickerson[5] describes the action of Apresoline as follows:

"A preferential effect on arterioles, as compared to veins, allows the increase in cardiac output and minimizes postural hypotension; the latter is much less than that produced by agents blocking sympathetic nerves."

Continued on following page

Apresoline® hydrochloride
(hydralazine hydrochloride)

TABLETS

INDICATIONS
Essential hypertension, alone or as an adjunct.

CONTRAINDICATIONS
Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease.

WARNINGS
Hydralazine may produce in a few patients a clinical picture simulating systemic lupus erythematosus. In such patients hydralazine should be discontinued unless the benefit to risk determination requires continued antihypertensive therapy with this drug. Symptoms and signs usually regress when the drug is discontinued but residua have been detected many years later. Long-term treatment with steroids may be necessary.

Complete blood counts, L.E. cell preparations and antinuclear antibody titer determinations are indicated before and periodically during prolonged therapy even though patient is asymptomatic. These studies are also indicated in the presence of any unexplained symptoms.

A positive antinuclear antibody titer and/or positive L.E. cell reaction requires that the physician carefully weigh the implications of the test results against the benefits to be derived from antihypertensive therapy with hydralazine.

Use MAO inhibitors with caution.

Usage in Pregnancy
The drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.

PRECAUTIONS
Use cautiously in suspected coronary artery or other cardiovascular diseases, cerebral vascular accidents, and advanced renal damage. Postural hypotension may occur, and the pressor response to epinephrine may be reduced.

Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an antipyridoxine effect and addition of pyridoxine to the regimen if symptoms develop.

Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported rarely. If such abnormalities develop, discontinue therapy. Periodic blood counts are advised during prolonged therapy.

ADVERSE REACTIONS
Common: Headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; angina pectoris. *Less frequent:* Nasal congestion; flushing; lacrimation; conjunctivitis; peripheral neuritis, evidenced by paresthesias, numbness, and tingling; edema; dizziness; tremors; muscle cramps; psychotic reactions characterized by depression, disorientation, or anxiety; *hypersensitivity (including rash, urticaria, pruritus,* fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis); constipation; difficulty in micturition; dyspnea; paralytic ileus; lymphadenopathy; splenomegaly; blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura; hypotension; paradoxical pressor response.

DOSAGE
Initiate therapy in gradually increasing dosages; adjust according to individual response. Start with 10 mg 4 times daily for the first 2 to 4 days, increase to 25 mg 4 times daily for balance of first week. For second and subsequent weeks, increase dosage to 50 mg 4 times daily. For maintenance, adjust dosage to lowest effective level.

The incidence of toxic reactions, particularly the L.E. cell syndrome, is high in the group of patients receiving large doses of Apresoline.

In a few resistant patients, up to 300 mg Apresoline daily may be required for a significant antihypertensive effect. In such cases, a lower dosage of Apresoline combined with a thiazide, reserpine, or both may be considered. However, when combining therapy, individual titration is essential to insure the lowest possible therapeutic dose of each drug.

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Tablets, 10 mg (pale yellow, dry-coated); bottles of 30, 60, 100 and 1000.

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Tablets, 100 mg (peach, dry-coated); bottles of 100.

Consult complete literature before prescribing.

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C I B A

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The Humanity of Our Courts

AGAIN, A COURT VERSUS the FDA. This time it was a United States District Judge in Oklahoma City who had previously ruled against the FDA, ordering FDA officials not to interfere with the importation from Mexico of Laetrile by a cancer patient. His latest order relieves hospital and physician of criminal liability if they administer the drug to the patient. We cannot suitably evaluate the legalities or the letter of the law; we can appreciate the humanity of the judgment.

There isn't the slightest doubt that the FDA's mandate enables it to deny a new drug application to a manufacturer to sell a medication in interstate commerce. The FDA may (we do not *know*) have proof that a preparation made from apricot pits has demonstrably harmful levels of hydrogen cyanide. Furthermore, the FDA is doubtless sound in maintaining that there is no well-controlled research demonstrating the anticarcinogenic efficacy of this preparation. But the court's finding was that all available evidence showed that Laetrile was harmless and "was not necessarily void of effectiveness." It went on to say that this may be limited to the hope that the patient may derive some benefit from it "but if the drug relieves his mind of pain, then it is effective."

Considering the multifaceted character of malignancies, it would be rash to conclude that no single individual may benefit either from a biochemical or psychic mechanism of a drug in which a patient deeply believes. There are certain situations in which judgment should be tempered by humanity, compassion, and tolerance, particularly for a patient who had been told that he had cancer of the rectum four years ago and has been taking a medication and is alive today and claims to be well as a result of it. Certainly for that individual the FDA's contention of "harmful effects of a drug" does not apply.

There is no question that reliance on questionable medications in treatable cases of malignancy defers the use of proper procedures and poses a threat to public health. Nonetheless, it would seem to us that an individual who wishes to continue to use a medication he believes in, even if the rest of the world does not, should have that personal right. No government agency prohibits people from exposing themselves to known, proven carcinogens. On the contrary, the U.S. government not only does *not* restrict the sale of such carcinogens as cigarettes but actually subsidizes the growth of tobacco.

The FDA acts within its province in refusing an NDA for Laetrile but, we believe, goes beyond the intent of the law and the bounds of good judgment when it harasses people who are seriously ill and believe their survival is dependent upon a medication of which the FDA disapproves. A.M.S.

Tumor Immunotherapy

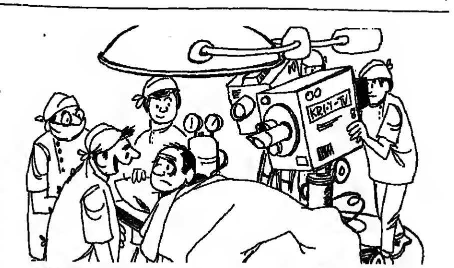
AS OF JUNE, 1975, the International Registry of Tumor Immunotherapy listed more than 200 protocol studies. Of these, as many as 74 are being sponsored by our own National Cancer Institute. Dr. Stephen K. Carter of the NCI's Division of Cancer Treatment observed at the International Conference on Immunotherapy that the approach "is the newest, and one of the most exciting, of the therapeutic modalities in the armamentarium of clinical oncology." It is no wonder that investigators are eagerly exploring its possibilities, but as Dr. Carter emphasized, we are a long way from its practical utilization and before that is possible there is a "tremendous amount of work that must still be accomplished."

The attractiveness of the concept that tumor cells bear distinctive antigens capable of "eliciting humoral and cell-mediated responses whose possible manipulation" may lead to tumor rejection, is undeniable. The avenues being explored are multiple and that alone is a complicating factor. But above all, Dr. Carter cites the observation that "immunity against cancer is relative rather than absolute." The normal host defenses can destroy what are relatively small numbers of tumor cells, of the order of one to 10 million, but a neoplasm one cm in diameter contains about one billion tumor cells. By the time tumors are clinically detectable, most have overcome immune defenses and "it is unlikely that immunotherapy alone will ever bolster host defenses sufficiently to reverse tumor growth in patients with advanced disease."

Most investigators agree that "the practical future of immunotherapy appears to lie in its role as part of a combined modality approach," that is, after surgery, radiotherapy and/or chemotherapy have succeeded in leaving behind only small numbers of tumor cells. But what the immunotherapeutic techniques are to be and how they are to be applied is still a long way off, so far as one can presently tell.

Sputum Cytology

CLINICAL QUOTE: *"These initial data offer some encouragement [that through sputum cytology] persons with presymptomatic lung cancer can be identified . . . and treated . . . Early results suggest long-term survival and possible improvement in the quality of life."* (Dr. D. Sanderson. See page 1.)



"This won't take long . . . We break for commercials in 15 minutes."

LETTERS TO TRIBUNE

Hyperbaric Therapy

MEDICAL TRIBUNE (Oct. 22) contains a very well written story of our hyperbaric hydrogen therapy for treating cancer. One slight correction: my coauthors, Dr. William P. Fife and Dr. F. Ray Wilson were listed as both being from the Department of Biology, Baylor University. Actually, Dr. Fife is a biologist at Texas A & M University and was indeed Chairman of the Department of Biology there for a number of years. . . .

MALCOLM DOLE, PH.D.
Robert A. Welch Professor of Chemistry
Baylor University
Waco, Texas

Meditating on Meditating

"Meditation without Metaphysics," (MT, Nov. 19) well summarizes the technique of transcendental meditation (TM).

The use of a mantra is an integral part of TM. It should be a meaningless word—otherwise it calls forth ideas which may disturb the orderly procedure. That is the reason why, I believe, the word "one" can serve only if it is pronounced to rhyme with "bone." Otherwise, one tends to lapse into counting—one—two—etc.

I have taken the standard course and believe that Dr. Herbert Benson has performed a service in making TM available without the trimmings. Incidentally, I have experimented with various mantra—and invariably found that words that have a meaning (like *sing, ran, sigh*, etc.) do militate against TM practice. Even another meaningless word, like *ha*, would be undesirable: think of saying *ha, ha* as you breathe in and out—you may well begin to laugh. Then you may laugh meditation out of practice.

ERWIN DI CYAN, PH.D.
New York, N.Y.

Costa Rica Anyone?

Much has recently been written about Costa Rica and the many American "Pensionados" (retirees) who have settled there. Had it not been for a bout with breast cancer, we would already be among them. Because of the excellent medical facilities in Costa Rica, I have been given the okay for our move to Guanacaste Province, near Liberia City.

We will soon be building our home in Ranchos Maricosta, where we will have a few cattle for the freezer, horses for our two children, a garden, and fruit and nut trees. It is a long-awaited dream—and we can hardly wait!

Cost of living is still so low and taxes there so nearly nonexistent we can live comfortably on my husband's modest Navy retirement pay. We can hunt in the nearby mountains, fish in the Pacific and, if we ever tire of that, we can play golf and tennis, or just laze around in the sun (as we used to be able to do in now-many-times-more-expensive Hawaii).

If any readers would like more information about this beautiful, amazing little country and its Retirement Law, they can write me.

MRS. LEWIS M. BIRO
7000 South Dent Road
Hixson, Tennessee 37343

One Man . . . and Medicine

Dr. Sackler's "One Man . . . and Medicine" remains the highlight of the MEDICAL TRIBUNE in our eyes.

Thank you.

W. P. ONDELHEIDE, M.D.
Loma Linda, Calif.

Gutenberg's Name

It is rare indeed to find an error—be it ever so miniscule—in Dr. Sackler's excellent articles. But sooner or later, it must—as to all of us—happen.

Johann's father's name was Gensfleisch, but the son chose his mother's maiden name Gutenberg. The spelling calls for just one T—no need to cross your T's twice.

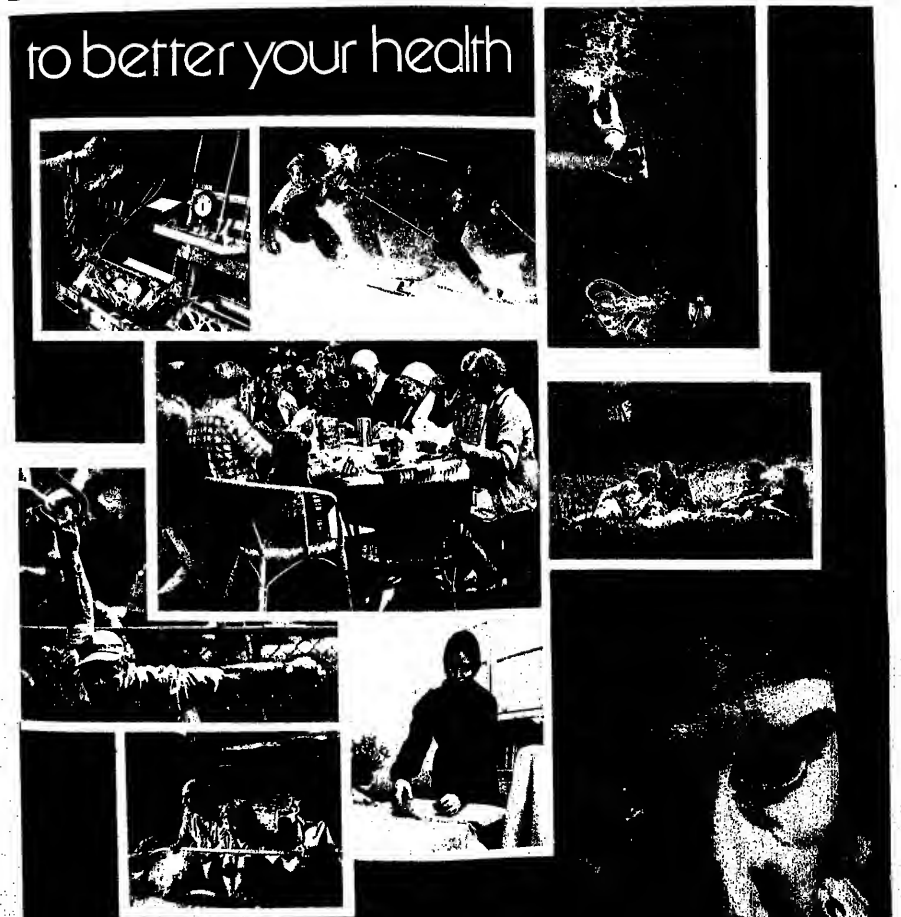
Please continue and for many years.

MELWYN BERLINO, M.D.
Brooklyn, N.Y.

Don't Miss
THE GOOD DRUGS DO
Edited by the famous clinical pharmacologist, Dr. Lasagna, designed to be removed from Medical Tribune for your waiting room, it begins on Page 9.
FOR YOUR PATIENTS

THE GOOD DRUGS DO

to better your health



Have you lost satisfaction in your work... family... hobbies?

You may be depressed without knowing it.

Medical Tribune
AN EDUCATIONAL SERVICE FOR PATIENTS

Clues to the Blues

Your enjoyment is lost in activities that were once exciting, satisfying and joyful. Bowling or baseball or hunting or skiing seem hardly worth the trouble anymore. Winning at bridge or poker or gin or pinochle is unimportant. Your hobbies, whether stamp-collecting, knitting and sewing, repairing machines or cooking lose their savour. As a depression deepens, more and more time may be spent reading or watching television, but eventually even these pastimes are no longer satisfying. Neither work nor anything else produces a feeling of accomplishment.

Your pleasure in your family and friends is reduced. No desire exists to visit anyone. If old friends phone, there is no pleasure in talking to them. Everything seems like "the same old thing." You may feel indifferent about your family, including your spouse and even your children. It is frightening at times to feel that no one is important any longer. Some people may, in depression, develop a real emotional anesthesia—complete indifference—about those who were once most dear.

Your fatigue may be so great that you haven't enough energy to get things done that used to be simple to accomplish. Everything seems "too much." You may also have feelings of weakness or dizziness, sweating, coldness or tingling of hands or feet, headaches, and other pains for which no medical cause can be found. You may suspect physical illness but the tests prove negative.

Continued on page 15

Medical Tribune

THE GOOD DRUGS DO to better your health

is specially prepared for the waiting rooms of America's physicians to provide patients with accurate information about drugs, vitamins and foods their physician may prescribe.

Dr. Louis Lasagna, Professor and chairman, Department of Pharmacology and Toxicology University of Rochester School of Medicine and Dentistry, is editor of this service.

Each installment features a leading authority on a health problem of concern to the public and to physicians.

Depression is treatable

By Nathan S. Kline, M.D.
Lasker Award Winner; Director, Rockland Research Institute, New York State Department of Mental Hygiene

Depressions are very much like infectious diseases in some respects. In both, medications are available which work remarkably well. And most patients with either condition tend eventually to recover even if not treated—although the process may be long and painful. Yet some patients do not get well unless treated.

Until 20 years ago only a limited number of things could be done to help the depressed person. In some cases psychotherapy helped. In more cases electroshock treatment, now in use about 35 years, helped. But in the early 1950s the first of a whole new group of medications which biochemically relieved depression were discovered. Today we even have means of helping to prevent depression from occurring.

Strange as it may seem, one of the unfortunate aspects of depression is that many people—particularly those who are depressed and their families—do not know that depression is treatable. The depressed person feels overwhelmed with hopelessness. His depression—his withdrawal and irritability—depresses everyone around him, and then things indeed seem hopeless. Today we can successfully treat depression in most cases and interrupt this vicious cycle, which often is destroying the life of an entire family.

Knowing that depression is treatable is a critical factor in altering such a situation, but the first step is recognizing the signs and symptoms in yourself or some member of your family.

We all have experiences that leave us sad and disappointed, that make us blue and depressed. Life is full of such ups and downs, and that is perfectly normal. But when no glad days occur, when one's blues become a fixed attitude, when life's satisfactions disappear, one can properly and accurately say: "I have a depression." When one is depressed about one aspect of his life, he may find that after talking it over with a friend or relative, with his

> **"Today we can successfully treat depression in most cases and interrupt this vicious cycle..."**

minister or doctor, he feels relieved. Talking with another person helps one gain a more objective and realistic view—even of things that are sad. Often this may be all that is needed. If this does not help, the person is almost certainly in need of treatment.

One question frequently asked is, "How can I tell what is ordinary grief or sadness from what you call depression?" The degree of pain experienced or the extent to which the depression interferes with normal activities is the best way of judging. In my opinion, three or four days of continuous agonizing depression or marked withdrawal from normal routines should be enough to warrant medical consultation.

The fact that there is a "reason" for feeling depressed doesn't justify being depressed for a long period of time. Most of us have plenty of reasons to be depressed but fortunately they do not result in a prolonged painful illness. Unrelieved continuous depression requires treatment even if there is a "cause" that can be identified.

Depression is probably as old as mankind, according to Biblical and other ancient records. And efforts to treat it are at least as old. In ancient Greece treatment with diet, rest, and an early form of psychotherapy was given in the Temple of Hygeia. When King Saul had his attacks of melancholy, David played the harp to ease him, according to the Bible. Mineral spring water was used in Roman times. Beginning in Greece, and later followed in medieval Europe, a theory was developed that depression was due to an excess of black (melan-) bile (-chol) so that patients with this condition were referred to as "melancholy." Today we know that there is no such substance as black bile, but there is scientific evidence that the chemical balance of the body is disturbed in depression. What our modern drugs do is to intervene in these chemical disturbances.

Freud's Concept

Dr. Sigmund Freud, who developed psychoanalysis, suffered from depression. He treated himself with the drugs then available. However, the drugs of that day were not regularly effective and safe. Later he and his followers developed a theory that depression developed when anger could not be expressed outwardly against the person causing it. In such cases it is turned inward against one's self and results in depression. Treatment with various types of psychotherapy, either alone or in combination with medication, is helpful in some cases.

One of the limitations of psychotherapy is the amount of time it takes and its cost. The number of people who are depressed is so large that this method cannot possibly be used for all of them.

The search for effective drug therapy has at times moved up blind alleys. For example, in the 1930's when it was found that the amphetamines, which are used as stimulants and for diet control, provided a short-acting "lift," some people thought they could be used against depression. However, their lift was usually followed by a crash into "the blues." Moreover, the body developed tolerance to them—so that to provide a "lift," they had to be used in increasingly larger doses—and at high doses their physical effects are most uncomfortable. In addition, in some patients, their continued use produced drug dependence. While these drugs, which are psychomotor stimulants, have a certain use in psychiatry, it is limited.

Electroshock therapy, sometimes called "ECT" or "EST," was first introduced in Italy in 1938. It had earlier been discovered that seizures or convulsions seemed to relieve depression in certain cases. Because of the tremendous need for some means of providing relief there was widespread use of this procedure, even though it sometimes caused a fracture and some temporary amnesia about recent events. Improvements in understanding the technique were developed. When patients were given "muscle relaxants," there were fewer problems with sore muscles and occasional fractures. Another refinement consisted of sending the current through only one side of the head, which eliminated the seizures and reduced the memory loss. However, its beneficial effects may not last.

Magnitude of Problem

The next great advance was the introduction of antidepressant medications in 1957 by me and my colleagues. Only 6 months later and entirely independently, Roland Kuhn in Switzerland reported on the first of another group of antidepressant drugs. The first group of medications, called monamine oxidase inhibitors (MAOIs, for short) seem to work by increasing the amount of a chemical which carries impulses from one nerve to another. The second group, named tricyclics, do the same thing but in a different way. In depression it may be that the chemicals transmitting nerve impulses are not produced in sufficient quantity or are destroyed too rapidly. The medications seem to correct this condition.

Continued refinements in these medications and their use has now made it possible for millions of depressed patients to be treated effectively by their physicians or specialists to whom the patients are referred.

> **"Continued refinements in these medications and their use has now made it possible for millions of depressed patients to be treated effectively..."**

However, one of the major problems is that many people who are suffering from depression do not know treatment is available. The magnitude of this educational problem is staggering. It has been estimated that 15 per cent of the adult population of the United States has some degree of depression which is serious enough to be in need of treatment. This amounts to about 20 million people, which makes it not only the most frequent psychological disorder but also one of the most common of all serious medical conditions.

One authority estimates that only 10 per cent of those seriously ill from depression are actually receiving treatment. Thus nine out of every 10 persons who are ill from depression receive no help.

What has led to this strange and tragic state of affairs? and what can be done to correct it? For one thing, many people who suffer from depression don't know what is wrong with them. Sometimes the symptoms are even harder to detect than the most common ones listed under "Clues to the Blues."

The person with a depression may be brought to attention because he or she is a chronic "underachiever." Only close questioning reveals an underlying depression which explains why the person never makes that extra little effort.

In part, a pessimistic outlook makes the depressed person "convinced" in advance that nothing can be done. Sometimes it is the lack of pleasure in accomplishment that stops him or her. At other times, the individual simply does not function effectively.

Depression may also show itself in other ways. Possibly in order to avoid the pain which depression produces, some people have "depression equivalents." For instance, some patients have obsessions (thoughts which they cannot get out of their heads) or they develop compulsions (acts which must be repeated over and over—such as checking time after time to be certain the gas in the stove is off, or that the door is locked). Sometimes there are strange fears or phobias. While there may be other causes for the obsessions, compulsions, and phobias, they are often produced by depression.

Depression and Old Age

Depressive, especially if it is accompanied by anxiety, can be so painful that the patient feels almost anything would be better. To get relief from their persistent "low" or "empty" feelings, such persons often end up taking all sorts of drugs (LSD, opium, morphine, cocaine) and especially alcohol. Properly treated with antidepressant medication, the frequency of drug addiction and alcoholism can be reduced.

"But you stood up to him. That's all that matters."

For this installment

THE GOOD DRUGS DO

turned to one of America's foremost authorities on depression, Dr. Nathan S. Kline. He won the Lasker Award for his discoveries of effective drug treatment of depression. Today he is director of the Rockland Research Institute at Rockland State Hospital in New York, Clinical Professor at Columbia University College of Physicians and Surgeons and a Fellow of the American College of Physicians and a Founding Fellow of the Royal College of Psychiatrists of England.

He also wrote *From Sad to Glad, Kline on Depression*, published by G. P. Putnam's Sons, New York, 1974. An advisor on mental health for the World Health Organization and former chairman of the American Psychiatric Association's research committee, Dr. Kline is also in private practice in New York.

Your Questions about Depression Answered

Is depression more common in women than it is in man?

Yes. It seems unfair but almost twice as many women as men become depressed. Medications work well in both groups but are somewhat more effective in man than in women.

Are antidepressant medications habit forming or addicting?

No. It is not the antidepressant medications but a different group of drugs, the stimulants, which may lead to development of drug dependency.

The confused linking of stimulants or "uppers" (amphetamines and related drugs) with antidepressants is not really justified since the stimulants provide a quick "lift" often followed by a "crash" whereas the antidepressants take about 3 weeks before their effect begins to be felt and there is no drug let down if their use is discontinued.

Is it necessary that I understand why I am depressed?

Sometimes **yes.** Usually **no.** In some cases the depression arises because of emotional problems and insight is useful. In most cases, especially of moderate or severe depression, it is not necessary to know why the depression exists. In fact, it may be difficult or impossible to find a psychological reason. The depression may be entirely the result of biochemical or physiological changes.

Is depression a rare condition?

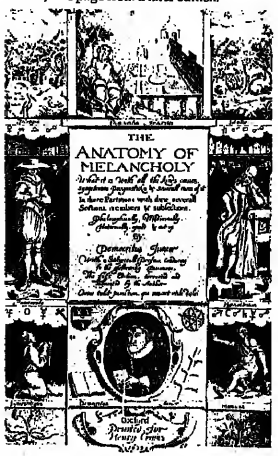
No. It is the most common of the psychological disorders and far more frequent than most physical illnesses.

Continued on page 14

Medical Advances in Overcoming Depression

Anatomy of Melancholy

by Robert Burton, published in 1621, was one of the first medical texts to examine the symptom causes and treatment of depression. Below, title page from a later edition.



Medicinal Plant

Plants, like rauwolfia serpentina—used for centuries in India to relieve anxiety—provided clues to modern medical scientists seeking to create drugs that would relieve depression and other emotional states.

Dr. Sigmund Freud who was himself often depressed, demonstrated the therapeutic value of having the depressed patient talk about what was troubling him. Through the patient's associations Dr. Freud was often able to recognize forgotten losses and disappointments which were contributing to the depression and feelings of worthlessness. Remembering these often helped the patient. Later psychiatrists developed other techniques, such as helping the patient become active in recreational sports, social affairs and hobbies to help overcome feelings of depression. Dr. Freud believed that a biochemical solution would be found for most psychoses.

Antidepressant drugs can prevent suicides

Situations like that shown above can be prevented. Usually the suicidal person will indicate how he feels. Questioning a person if he feels suicidal does not suggest it, as many people fear, and is an important step in preventing it. Anyone may feel at some point that life is not worthwhile, but talking to someone helps. This is why "Suicide Hotlines" have been set up in many cities. A physician can not only listen to such troubles, but he can provide drugs which will ease the crisis.

Shock Treatment

Italian physicians discovered in the 1930s that severely depressed patients could be helped with the use of mild electrical shocks to the brain. Considerably improved, with the shock reduced, and aided by muscle relaxant drugs, this form of treatment is still used in severe cases.

The Gloomy Dane

In *Hamlet* Shakespeare dramatized the paralyzing character of depression.

Stopping the Up-Down Cycle of Depression

The Australian physician, Dr. John Cade, recognized that lithium appeared to help patients who went through cycles of being very depressed and then very active and full of energy. Other medical scientists then helped to refine the use of lithium so that today it is used to prevent these wide swings in mood. Meanwhile in Washington, Dr. William Hamaty and other medical researchers used studies of such depressions to discover that there is a biochemical warning of the swing from "blue" moods to "high" ones. This has greatly encouraged scientists to believe that full control of depression through drugs is close at hand.

Anyone can be depressed

No one—not even spaceman—is immune to depression and no one should be ashamed of feeling "blue". Astronaut "Buzz" Aldrin, third astronaut to walk on the moon, felt overwhelmed by the endless round of emotionally draining public appearances on returning to earth. Depressed, he had the courage to say so and seek treatment.

Babies need approval

These pictures are from a research movie made by Dr. Rene Spitz proving that the infant responds even to a face painted on a balloon.

Your Questions about Depression Answered

Continued from page 11

How long does it take for the medication to work?

Three to four weeks is about the average time required for antidepressant medication to *begin* working but if a low starting dose is used it may take even longer. It is important to realize that there may not be any advance evidence of improvement and patients should not be discouraged if no change is noted for the first 3 to 4 weeks. Once improvement begins, it usually continues quite rapidly and within another month the patient is recovered.

Can I have a depression without feeling depressed?

Yes. Sometimes, in order to protect herself or himself against the anguish of a depression, an individual will attempt to "bury" such depressed feelings and will then develop other symptoms, even physical ones, which substitute for the depressed feeling. A headache or a stomachache may be such a substitute in some cases. Physicians call this a "masked depression."

Do antidepressant medications have side effects?

Yes. Any drug potent enough to be useful almost always has some other action as well. This is true of drugs for arthritis and heart disease as well as for depression. The antidepressants often produce dryness of the mouth, sometimes constipation and occasionally other side effects.

Compared with most medications, the antidepressants are quite safe and their side effects either disappear with continued use or when the drug is discontinued.

Is depression inherited?

We don't know. There is a tendency for certain families to have more depression than others but it doesn't follow the usual pattern of inherited diseases. We're not certain as to why one member of a family becomes depressed and another does not.

Is depression an inevitable part of growing old?

This is not true. Most people who are going to have depressions will have had the first episode long before they are sixty or seventy. Part of the problem is that we sometimes expect older people to be very quiet or depressed —and we almost discourage cheerful and happy behavior among them by our expectations. We don't encourage them to be active. Given half a chance many elderly people will enjoy the same movies, television, sports, jokes, picnics and other experiences—just as younger people do. If they don't, it may well be that they are depressed and in need of treatment.

What your doctor can do

If you feel depressed, your doctor can determine if you need treatment. There is no blood test to diagnose depression. Therefore, the decision as to whether your symptoms add up to a disorder for which medication or some other treatment should be given must be made by your doctor or the specialist to whom he refers you.

In part, your doctor's diagnosis is based on how severely you are suffering and the degree to which your functioning is crippled.

Almost everyone thinks of committing suicide at one time or another. This can be frightening and depressing in itself. Your doctor can help you distinguish whether or not you are really suicidal. That this idea may have occurred to you should certainly be mentioned to your doctor. But it does not necessarily mean you are suicidal. When you talk about it be sure to explain: 1) whether it is just a thought that passed through your head; 2) whether you wish you were dead but don't feel strongly enough to try and do something about it; 3) whether you wish you were dead and do feel strongly enough to try and do something about it; 4) whether you *don't* really want to be dead but are afraid you may try to do something; 5) whether you are in a most uncomfortable or anxiety-producing or upsetting situation that you feel you simply can't stand another 24 hours—even if you have "to kill yourself" in order to get it over with, because your doctor can give you some medication to provide great relief for anxiety *rapidly*; 6) whether you are angry or disappointed or guilty about something that happened between you and someone else, someone whom you feel would react to your being "dead" by feeling sorry or angry or upset.

> "Unrelieved continuous depression requires treatment even if there is a 'cause'..."

Your doctor can also help decide whether your hospitalization is desirable. Many patients are afraid of being "put away" in an institution. Often, however, it is a great relief not to have total responsibility for yourself and what happens. It also can make things easier by temporarily separating you from your problems in living and working. Reducing the immediate pressure in this way can provide great relief. Sometimes patients feel that some other person is involved in provoking or causing his illness and going into a hospital provides an "escape."

If medications are needed they can often be given in much higher doses—and responses may be more rapid—in a hospital setting. Fears of patients that they will be "locked away" forever are unrealistic. All sorts of legal safeguards exist to protect the patient. In any case hospitalization is rarely needed today.

Your doctor will usually explain the nature of the medication he is giving to you. Most antidepressants take about three weeks to *begin* to work and another few weeks before the full effect starts to be felt. The antidepressant medications are very much like the antihistamines—sometimes the first medication doesn't work and two or three have to be tried.

With a few of the antidepressant medications a diet must be observed—certain foods and medications are limited or eliminated. If you are given one of these medications your doctor will give you a list of the foods and drugs to be avoided. There are certain diseases, such as one type of glaucoma, in which medications must be used with caution, so be certain to give your doctor a list of any previous illnesses.

The side effects of the medications are usually more annoying than serious. Dryness of the mouth and some constipation are the most common. For the first few days there may be some sleepiness and occasionally a patient may feel a bit unusual or peculiar for a short time. Sometimes there is a little "lightheadedness" or dizziness which you should let your doctor know about.

Let Your Doctor Know

The decision about what drug to use depends on what symptoms you have and your medical history. If you have had previous depressions, it is useful to be able to give the doctor [illegible] information about when the depressions occurred and how you were treated, that is, how much of which drugs. However, this information is [illegible] absolutely essential. It is essential to see your doctor even if you don't [illegible] all the details of any past treat[illegible]

Once your symptoms are gone, [illegible] doctor has several decisions to [illegible] He may decide that medication [illegible] gradually be reduced and then [illegible] tinued. Sometimes it is advisable [illegible] remain on a low "maintenance" [illegible] for quite a while. If you have had [illegible] vious depressions, your doctor [illegible] cide to place you on lithium.

Lithium acts as a kind of "[illegible] policy" against recurrence. In a[illegible] 15 per cent of the cases it doesn't [illegible] However, in 15 per cent it works [illegible] mediately and completely, and in another 70 per cent of the cases the patient becomes better able to deal with depression as time goes on.

During the first six months there [illegible] be recurrences. It is important to [illegible] this because if another episode of de[illegible] pression occurs the patient may [illegible] "the drug isn't working." The pro[illegible] really would be that the pa[illegible] been on the drug long enough [illegible] narily the doctor will continue [illegible] lithium and add an antidep[illegible] medication. The antidepressant [illegible] discontinued gradually after the [illegible] pression is over but the lithium [illegible] continued.

Your doctor can explain to the [illegible] and friends that depression has a [illegible] "favorable prognosis" which [illegible] that there is a great likelihood the [illegible] outcome of treatment will be [illegible]

Your doctor can treat depr[illegible]

Depression is not an inevitable part of growing older. However, in older people the diagnosis of depression can be easily missed and as a result their condition may be unnecessarily complicated and inadequately treated. If someone has arteriosclerosis of the brain or symptoms of senility, the presence of depression may make the symptoms of arteriosclerosis or senility worse. It may be difficult to detect the depression. Yet when antidepressant medication is used and the depression clears up, the person is able once again to compensate for the other disorders and can function effectively.

Other conditions may at times resemble depression (for instance schizophrenia, hysteria, certain neurological disorders). If the patient is actually depressed but is misdiagnosed as having one of these other indicated conditions, then antidepressant treatment will not be given and the patient may continue to be ill for a long time.

In some instances, fear keeps people who are depressed from proper treatment. One such fear, which has been heightened by the hysteria about drugs in this country, is that the drugs may produce dependence. If this does happen, it is so rare that it has no ordinary significance in clinical practice.

Patients sometimes worry that if they once start to take medication they can never stop. This is completely untrue. A patient can stop completely at any time without ill effects, although of course it is possible that the depression may come back. It would be like a fever in which aspirin is used to relieve the elevated temperature. If the aspirin is stopped before the disease is cured, the fever will return. At the very worst one can restart treatment.

> "Most antidepressants take about three weeks to *begin* to work..."

Built-in Self Defeat

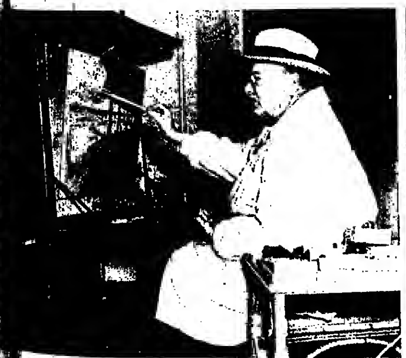
Self-defeating behavior seems to be built right into the fibre of depression. The unfavorable evaluation of one's self that is a characteristic of depression often prevents treatment. This is not the curious case of an isolated individual but one of the main factors preventing treatment for millions. Such people feel that they aren't worth treating, that they don't deserve the time, effort and money required. Often they feel so depressed that they feel the treatment won't work in their case even if it cures everyone else.

Curiously, there are also many people with the mistaken idea that emotional or psychological problems cannot or should not be treated with medication—it is too easy. They are convinced that they should suffer or somehow force themselves to feel better. This is truly foolish since no one wants to be ill and if it were a matter of wishing or will power there would be no illness—either physical, emotional or mental. Most people don't try to "pull themselves together" for pneumonia or a broken leg—they go to a physician for help.

Finally, there are those who "don't believe in drugs" or who worry unduly about side effects. Whether one should or should not use drugs for pleasure is open to discussion, but not to use medication for treating a serious illness such as depression would really be immoral.

Not only is it possible to treat depression successfully in 85 to 90 per cent of cases, but we now have a powerful new weapon in the fight against mental illness: a simple substance called lithium, which is usually capable of preventing the recurrence of most types of depression (not just manic-depression) or of markedly reducing the symptoms. Even if the depression should recur, the patient will almost always be able to continue to function. In such cases small doses of the antidepressant drugs, when added, are usually sufficient to relieve all symptoms rapidly.

In the treatment of emotional and mental disturbances, modern medical science has reached the point where the treatment of depression has achieved a high degree of effectiveness. After centuries of suffering, we now have great success in quickly relieving depression in the man or woman suffering so unnecessarily.



Famous people who overcame depression

Many famous people have suffered intensely from depression yet gone on to achieve great goals. Abraham Lincoln suffered recurring depressions, beginning in young manhood.

Nathaniel Hawthorne became so depressed learning to write, that for 12 years he rarely left his room. He wrote Longfellow: "I have secluded myself from society; and yet I never meant any such thing. I have made a captive of myself and put me into a dungeon, and now I cannot find the key to let myself out."

Winston Churchill took up painting to relieve his anxious depressions. He called his depressions "my black dog." Once, "for two or three years, the light faded out of the picture... I sat in the House of Commons but black depression settled on me."

Much of their suffering could have been relieved if modern drugs had been available.

Clues to the Blues

Continued from page 10

You may have insomnia frequently. It may be of the type in which there is a great deal of difficulty in getting to sleep. But sometimes going to sleep is no problem but then, after a few hours, sleep is fitful with constant restlessness, awakenings and dozing, for the remainder of the night. One very common pattern is one in which getting to sleep is not a great problem but there is "early morning insomnia." The patient awakens at 3 or 4 a.m. feeling depressed and anxious about many things—which he feels he cannot do anything about.

Your interest in sex and sexual activity may be decreased or absent.

Your loss of appetite may lead to loss of weight. If this is combined with constipation, you may suspect some serious disease, such as cancer, and gloomily accept that suspicion as true—as something "nothing can be done about." All this is exaggerated by your "doomed" outlook.

Anxiety adds to the discomfort. Most people with a depression also have anxiety which makes for a very uncomfortable state. Often they are so anxious or "nervous" that they cannot sit or rest comfortably. At times they are very frightened without knowing why.

The irritability of the depressed person often makes it difficult for those living with him or her. Despite general lack of interest and indifference about life in general, persons with a depression are easily irritated and tend to become angry with other people, even when they are trying to be helpful.

Do you feel guilty? Part of being depressed is to feel that there were many things you did in the past that you should not have done—or that you did not do things you should have done. In both cases the events are usually magnified and were actually unimportant or trivial. You may also feel guilty because you are not functioning as well as you could due to the depression. In addition, most people with depression feel guilty because they recognize that they have withdrawn their affection and no longer feel as strongly toward their loved ones as they did in the past. Fortunately, as the depression is relieved, the feelings of guilt disappear.

No one person has all of the symptoms listed in "Clues to the Blues." Some may have a few symptoms very intensely or a variety somewhat more mildly. One symptom may not be sufficient to make the diagnosis but should arouse concern. Because some symptoms occur in other diseases, professional help may be needed for a correct diagnosis.

What you can do to help yourself

YOU ARE NOT ALONE! Nor is your case unusual! About 20 million adults in the United States suffer—roolly suffer like you—from depression. Mental ond cmotiounl disorders ore *extremely* common. Yet the sad fact is that probably only ono of every 10 persons ill of depression goes for treotmant.

Recognizing thet you are dopressed and nead help is the first step in recovering your ability to onjoy lifa.

Even reading this nrticle moans you ore for better off than the avorsge person since you now stand a much better chonce of recognizing if you have'e depression and of going for trentmant. Since 85 to 90 per cent of patients respond woll to treotment, by going for holp you can reduce the amount of suffering both for yourself and those around you. Knowledge that you *can* and *will* get bettor changes everything.

Probably tho most important thing o petieot can do to be of help is to follow the doctor's orders exactly as directed. Sometimes petients feel they are doing something helpful if they take less medication then the doctor prescribes

"Recognizing that you are depressed and need help is the first step in recovering..."

or if they stop before they are supposed to. Exactly the opposite is true. Taking too low e dose moy result in the treatment taking much longer to work, or in achieving only partial relief of symptoms. Stopping too soon, even though the symptoms heva disappeared, may result in a recurrence.

Ooe of my patients told about her treatment on telcvision and received hutidreds of lettero. She replied to those who wrote to her thet:

1. Drug trentmoot worked for her when all other treotment had failed, but it did not solve all of her problems. Initially, her depression was so strong that it overwhelmed everything else. But when her'd depression was relieved, she was then much better able to deal with her other problems.

2. Always follow the doctor'a orders.

3. "Remember that it takes several weeks for antidepressnt drugs to work. Taking pills for only s few doys won't immediately relieve your symptoms."

4. "Tbere may be uncomfortable side effects at tha beginning of treatment but 'hang in there' and give your body a chance to adjust. It is e small price to pay for relief of the agony of dopression."

5. Don't take any othor medications unless you check with your doctor.

6. Don't stop taking your modication becauso you feel better. Only your doctor should mako that decision. Thero is nothing wrong with taking modication for n long pariod of tima if it is neodod. Many peopla feel it is a sign of weakness to "depand on a drug" but no one makes judgmonts about s diebotic's character because he or she uses insulin. "I certainly feel no guilt or lack of strength because I take n medicntion which my body needs and whioh nllows mo to be e productive and mentally healthy human being."

7. Lithium and antidepressont drugs are not addictive or habit forming.

8. "Don't feel ashamed or blame yourself for being depressed. And don't make the mistake of believing that your recovery is something you have to eccomplish by yourself."

9. "You will feel frightened and disheartened when you feel low after having experienced some comparatively good days. Just remembor that you are one of millions of people who are walking this path and that there seems no othor way to be completely well....

"I finally learned to really utilize the days when I felt well and to concentrate on the future when I felt 're-depressed.' I know of no other way. Just remember that there are good days now—not loog ago all was hopeless."

10. Drug therapy is n relatively inexpensive approach to the problems of depression. Bot if you need finmcial assistance, don't besitate to call your local Mental Health Association, State Department of Mental Health, Department of Welfare or perhaps your synagogue or church.

11. "I have directed my statements to you who are suffering the agonies of depression because you are my first concero. But I hopo you will shara my remarks with those who cara about you and who want to help. Just remember that although they don't understand (and most don't), they *do* want to help and often do not know what will be must benaficial unless you inform thea or osk them for holp."

How the family can help

LIVING WITH a person who is suffering from a dapression is very trying. Soon everyone is deprassed to some extent—but onlika tha peraon in the grip of tha depressive syndrome, they retain soma objectivity and the fooling that life is worth living. However, tha withdrawal and irritobility of tha depressed person, his or her rojoction of loving ottention, often makes trying to help seem usoless.

Betty Hamilton, who recovered from her depression with tho holp of drug treatment, wrote somo guidelines for families struggling with this problem.

"Trying to help a depressed porson who is often changeable ond unronsonsbla is a lonely, baffling oxporienca....

"But keep in mind wo are no longor living in the Dark Ages...and there are oow effective end lasting treatments for depressive illness. So the most significant contribution you can make is to help the depressive you care about find that treatment."

In addition:

a. Strivo to understand that life, for tho dopressivo, is full of an overwhelming ogony ond hopelessness and fear. Doing physicnl things for him or her, like cooking a moal, or even answering the tolophone will be a loving and helpful gesiore.

b. Don't advise that "if you only will get hold of yourself, everything will be all right." This advica is as ridiculous for tho dopressivo as it would be for the porson suffering from appendicitis.

u. Be potient. My husband, Paul, tells mo he used to pray for patience in my prosance and then cuss like mad nftor he had laft me. I suspect that both tho prayers and tho cussing helped him.

d. Anyono who threatens suicide should ba carafully watched and assisted in finding profossional help immediately.

e. Your constant assurance that help is available and that the patient will get well is n vitnl contribution.

Ismelin® sulfate
(guanethidine sulfate)

Esimil®
guanethidine monosulfate 10 mg
hydrochlorothiazide 25 mg

> **WARNING (Esimil)**
> This fixed combination drug is not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

INDICATIONS
Ismelin
Moderate and severe hypertension either alone or as an adjunct.
Esimil
Hypertension. (See box warning above.)

CONTRAINDICATIONS
Guanethidine: Known or suspected pheochromocytoma; hypersensitivity; frank congestive heart failure not due to hypertension; use of MAO inhibitors.
Hydrochlorothiazide: Anuria; hypersensitivity to this or other sulfonamide-derived drugs. The routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous.

WARNINGS
Antihypertensives are potent drugs and can lead to disturbing and serious clinical problems. Physicians should be familiar with all drugs and their combinations before prescribing, and patients should be warned not to deviate from instructions.
Guanethidine

> Warn patients about the potential hazard of orthostatic hypotension, which can occur frequently and is most marked in the morning and is accentuated by hot weather, alcohol, or exercise. To help prevent fainting, warn patients to sit or lie down with onset of dizziness or weakness, which may be particularly bothersome during the initial period of dosage adjustment and with postural changes. The potential occurrence of these symptoms may require alteration of previous daily activity. Caution patients to avoid sudden or prolonged standing or exercise while taking the drug.

Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression.
If possible, withdraw therapy 2 weeks prior to surgery to reduce the possibility of vascular collapse and cardiac arrest during anesthesia. If emergency surgery is indicated, administer preanesthetic and anesthetic agents cautiously in reduced dosage and have oxygen, atropine, vasopressors, and IV solutions ready for immediate use to treat vascular collapse. Vasopressors should be used with extreme caution in patients on guanethidine because of the possibility of augmented response and the greater propensity for cardiac arrhythmias.
Dosage requirements may be reduced in presence of fever. Exercise special care when treating patients with a history of bronchial asthma, since their condition may be aggravated.
Hydrochlorothiazide
Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.
Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte imbalance may precipitate hepatic coma.
Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.
Sensitivity reactions are more likely to occur in patients with a history of allergy or bronchial asthma.
The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.
Usage in Pregnancy
Guanethidine: The safety of guanethidine for use in pregnancy has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient.
Hydrochlorothiazide: Usage of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.
Nursing Mothers
Thiazides cross the placental barrier and appear in cord blood and breast milk.

PRECAUTIONS
[illegible]: The effects of guanethidine are cumulative over long periods; initial dose should be small and increased gradually in small increments. Use very cautiously in hypertensives with renal disease and nitrogen retention or rising BUN levels; coronary disease with insufficiency or recent myocardial infarction; cerebral vascular disease, especially with encephalopathy. Do not give guanethidine to patients with severe cardiac failure except with extreme caution.
In incipient cardiac decompensation, weight gain or edema may be averted by the administration of a thiazide. Remember that both digitalis and guanethidine slow the heart rate.
Peptic ulcers or other chronic disorders may be aggravated by a relative increase in parasympathetic tone.
Amphetamine-like compounds, stimulants (eg, ephedrine, methylphenidate), tricyclic antidepressants (eg, amitriptyline, imipramine, desipramine) and other psychopharmacologic agents (eg, phenothiazines and related compounds), and oral contraceptives may reduce the hypotensive effect of guanethidine. Discontinue MAO inhibitors for at least one week before starting guanethidine.
Hydrochlorothiazide: Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Observe patients for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis, and hypokalemia). Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbance such as nausea or vomiting.
Hypokalemia may develop with thiazides as with any other potent diuretic, especially during brisk diuresis, when severe cirrhosis is present, or during concomitant administration of steroids or ACTH.
Interference with adequate oral intake of electrolytes will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity.
Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients [illegible] therapy is [illegible] rather than administration of salt, except in rare instances [illegible] hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.
[illegible] elevations in plasma calcium [illegible] receiving [illegible], particularly in those with [illegible]. Pathological [illegible] parathyroid gland have been reported in a few patients on prolonged thiazide therapy.
[illegible] may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration.
Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.
If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.
Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

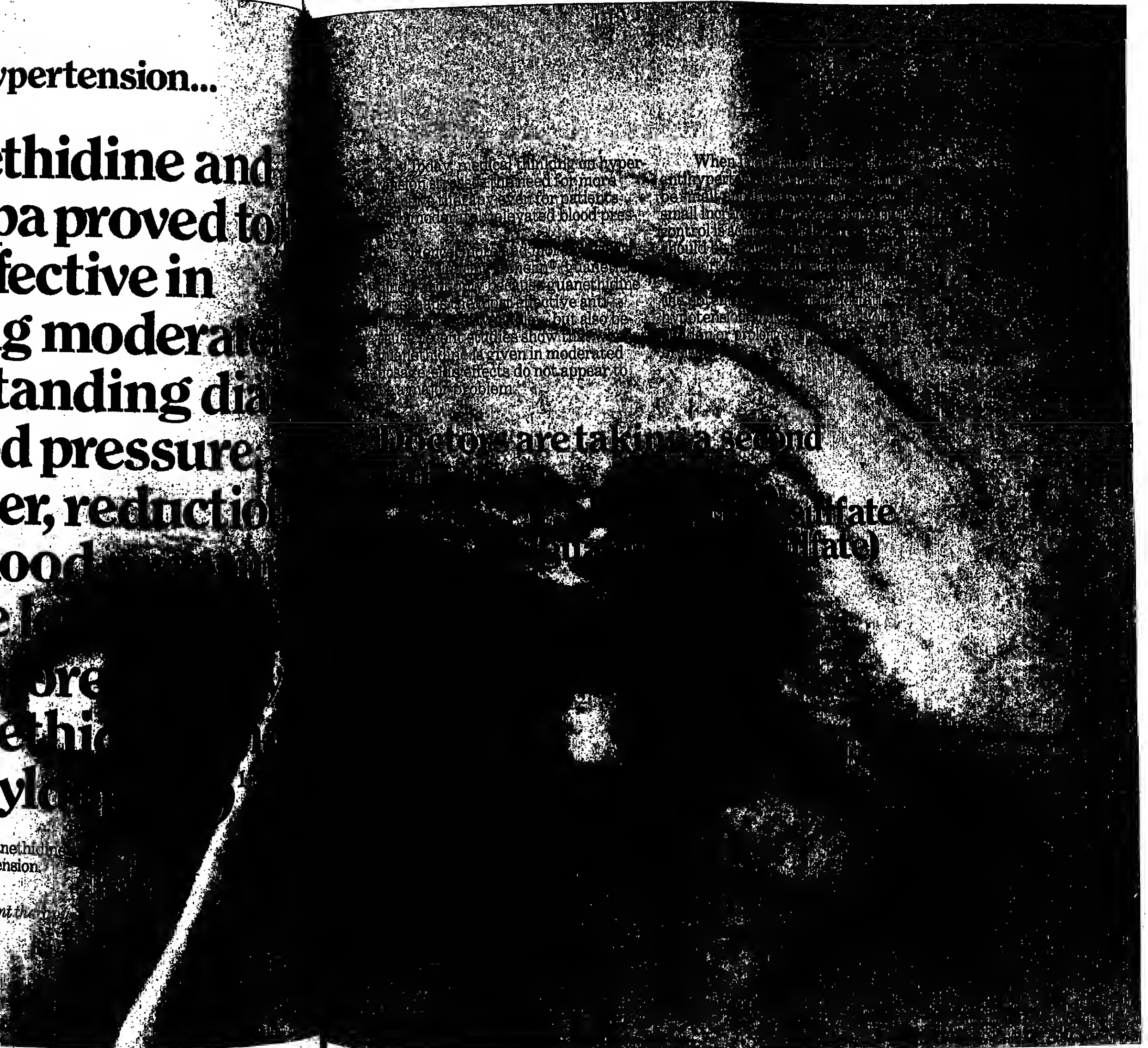
ADVERSE REACTIONS
Guanethidine: Frequent reactions due to sympathetic blockade—dizziness, weakness, lassitude, syncope. *Frequent reactions due to unopposed parasympathetic activity*—bradycardia, increase in bowel movements, diarrhea (may be severe and necessitate discontinuance of the drug).
Other common reactions—inhibition of ejaculation, fluid retention, edema, congestive heart failure. *Other less common reactions*—dyspnea, fatigue, nausea, vomiting, nocturia, urinary incontinence, dermatitis, scalp hair loss, dry mouth, rise in BUN, ptosis of the lids, blurring of vision, parotid tenderness, myalgia, muscle tremor, mental depression, chest pains (angina), chest paresthesias, nasal congestion, weight gain, and asthma in susceptible individuals. Although a causal relationship has not been established, a few instances of anemia, thrombocytopenia and leukopenia have been reported.
Hydrochlorothiazide: Gastrointestinal—anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic), pancreatitis. *Central Nervous System*—dizziness, vertigo,

(Brief prescribing information continued on next page)

In moderate hypertension...

"Guanethidine and methyldopa proved to equally effective in controlling moderate elevated standing dia stolic blood pressure.

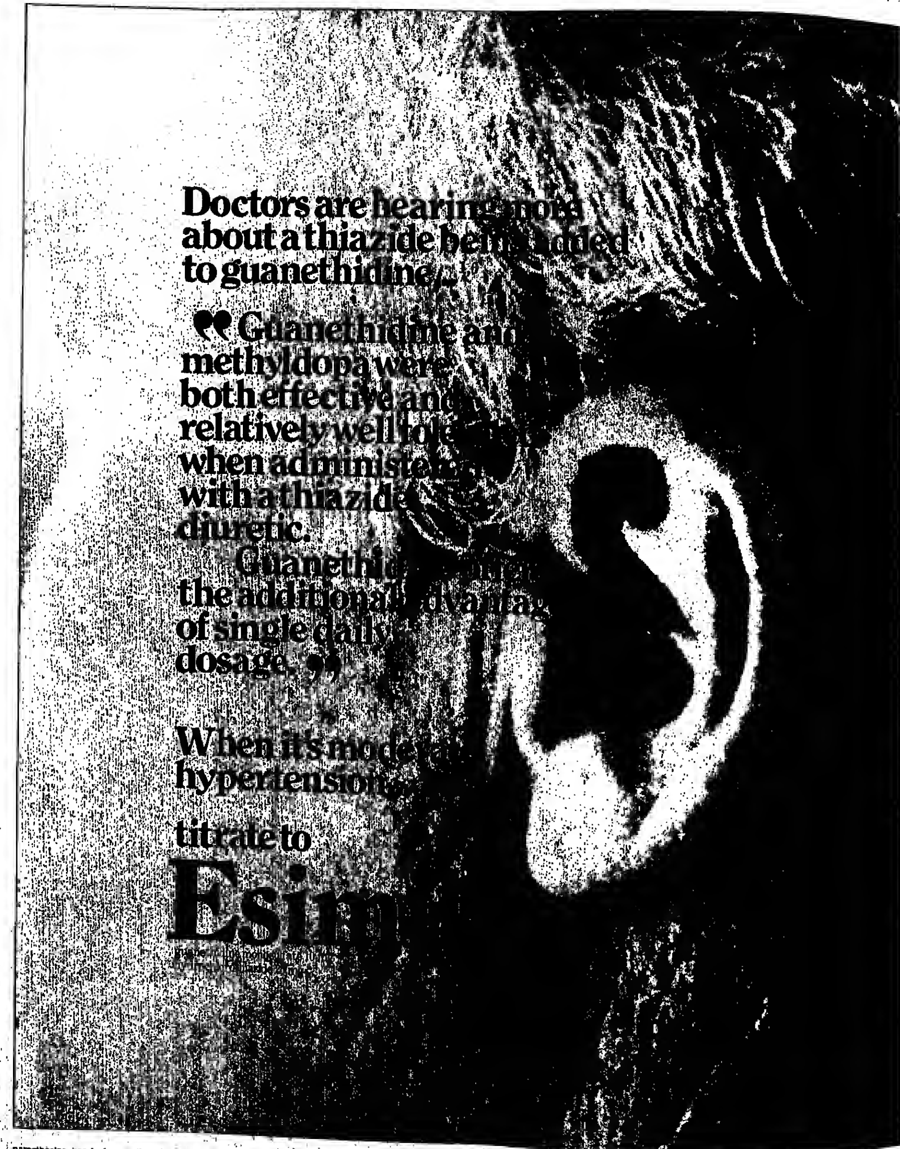
However, reductio of mean blood acceptable l achieved more with guanethi with methyl



1. Tarpley EL: Controlled trial of guanethidine and methyldopa in moderate hypertension. *Curr Ther Res* 16:1187-1196, 1974.

*All patients also received concomitant th[...] with hydrochlorothiazide.

C I B A



References
1. Tarpley EL: Controlled trial of guanethidine and methyldopa in moderate hypertension. *Curr Ther Res* 16:1187-1195, 1974.
2. Nies AS: Adverse reactions and interactions limiting the use of antihypertensive drugs. *Am J Med* 58:495-503, 1975.
3. Frais ED: *The Modern Management of Hypertension*, US Government Printing Office, 1973, pp 13, 14.
4. Langford HG: Hypertension, in Conn HF (ed): *Current Therapy*. Philadelphia, The WB Saunders Co, 1973, p 201.
5. Briggs AH, Holland WC: The cardiovascular system: Antihypertensive drugs, in DiPalma JR (ed): *Drill's Pharmacology in Medicine*, ed 4. New York, McGraw-Hill Book Co, 1971, pp 853-868.
6. Glazer N: Comparison of guanethidine and methyldopa in essential hypertension: A controlled study. *Curr Ther Res* 17:249-256, 1975.

One Man ... and Medicine

ARTHUR M. SACKLER, M.D.
International Publisher, Medical Tribune

The Three "Horsemen of Death"

Alcohol, Tobacco and Firearms

The Treasury Department's Bureau of Alcohol, Tobacco and Firearms announced recently that it would not require the listing of ingredients on labels of alcoholic beverages—News item.

FOR YEARS, we have been baffled by the government's evasion of its legal responsibility through the device of "baptising" alcohol as a food despite its clearly addicting potentials and its pharmacologic as well as toxic effects. To call alcohol, to which 9 million Americans are seriously addicted, a "food" and to simultaneously regulate prescription drugs, some of which are important in therapeutic regimens for managing alcoholism, is blatant hypocrisy—and a regulatory farce which sets logic on its head.

With a few rare exceptions (such as Dr. Theodore Cooper, Assistant Secretary for Health, and Dr. Morris E. Chafetz, former director of the National Institute on Alcohol Abuse and Alcoholism), U.S. health officials in the past have turned their backs on *disease causing* alcohol while they piously ply their attacks on medical *therapies* whose problems, at worst, are as "pimples" compared to the "cancer" of alcoholism.

The Nonregulatory Treasury

For years we noted that most of the new consumer advocates and public interest groups had failed to engage the issue or to promote balanced perspectives on the priority of our public health problems—particularly as they relate to alcohol. Be that as it may, the Center for Science in the Public Interest, through its Associate Director, Dr. Michael Jacobson, did enter the fight in 1972. It has charged that a government agency—the Treasury Department's Bureau of Alcohol, Tobacco and Firearms—is going completely beyond its authority and flaunting the law by ignoring the requirements of the Food, Drug and Cosmetic Act.

The Treasury Department's Bureau of Alcohol, Tobacco and Firearms has regulatory responsibility for three of the major causes of preventable mortality and morbidity in the United States. Incredibly, that bureau appears to act more as a nonregulator of the Three Horsemen of Death and Disability—alcohol, tobacco and firearms—than as a protector of the public whose interests are entrusted to it.

Reasons for No Action

Unbelievably, the bureau now gives as its reasons for non-action the excuse that the listing of ingredients in alcoholic beverages would "confuse" the consumer, cost him money, and that there is no indication it is desired by the public. For a government agency to make such a statement in the face of the nit-picking requirements for labeling and package inserts for safe and effective therapeutic, not recreational, agents, goes beyond the realm of comprehension, if not decency.

From its founding, MEDICAL TRIBUNE's editorial credo has addressed the need for perspective as well as for constructive action on alcoholism. It has pointed out the fact that alcohol and tobacco are two of the most addicting and toxic substances known to man. The toll of alcohol is massive. Of all automobile fatalities (over 50,000 deaths per annum), 50% are associated with high alcohol blood levels. Also, in respect to mortality, cirrhosis of the liver is the fifth leading cause of death for men in the productive years from 25 to 64. Alcoholism is implicated in malignancies such as cancer of the esophagus; its neurotoxicity is both cerebral and peripheral; its reduction of resistance to infection and trauma is notorious. In social terms, it is not only a destroyer of careers, it is a disruptor of the home (eight-fold greater frequency of divorce), and major contributor to addiction in the young.

Preventable Problems

In youth, alcohol is the first and probably most important drug of abuse as it may be the initiator of addiction to hard narcotics and multiple drug abuse. In economic terms the loss of life and limb are superimposed upon fires and home accidents. Work days lost from alcoholism are estimated at 44 million per year. However, it would appear that a government so vigorous in the pursuit of nonaddicting, noncarcinogenic, nonneurotoxic, noncardiotoxic drugs has little appetite for taking on the one drug which actually accounts for one of the two greatest causes of preventable mortality and morbidity in the United States.

Belatedly, but happily, we now hear from the FDA that "more informative labeling is in keeping with the best interests of the consumer." Considering the showing of regulatory muscle in the late cyclamate fiasco and the earlier cranberry bog, one wonders what could have accounted for the past apathy at the FDA in regard to the proven, toxic and addictive drug or so-called "food", alcohol. One must marvel at the regulatory intellectual footwork which first enables a government to side step regulating alcohol as a drug because it is a "food", and then to side step and avoid regulating alcohol as a food by having this responsibility delegated to a non-acting Bureau of Alcohol, Tobacco and Firearms.

That bureau is currently in default in respect to regulatory action on two other major killers and cripplers—tobacco, whose victims are marked in the scores of thousands, and firearms, a major vehicle for death by suicide and death by assault. It would appear that the "Horsemen of Death and Disability" through alcohol, tobacco and firearms have little to fear from the bureau of a government department which at the same time garners high tax income from the sale of two of these highly toxic agents.

What Is Needed

In view of the fact that Treasury may have either a "conflict of interest" or a "conflict of conviction," it is fitting that the Department of Health, Education and Welfare (whose funds are depleted in caring for the ravages of these dangerous agents) should take over. Two things appear clearly evident. We will watch with the greatest interest whether that which is obvious and that which is right will come to pass:

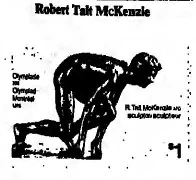
1. The FDA should act on its responsibility for the labeling of alcohol. This can be done immediately in accord with its agreement with Treasury's Bureau of Alcohol, Tobacco and Firearms.

2. Leaders in Congress in the forefront of national health issues such as Nelson, Kennedy, Fountain, Rogers and Moss can immediately set legislative hearings on this most vital of health issues.

More lives can be saved by simple legislative action (and it need not be prohibition) for better control of just three items—alcohol, tobacco, firearms—than could possibly be saved by a mass of other legislative activity. In the full perspective of the public health, to control therapeutic procedures and leave uncontrolled dangerous recreational agents is to offer the shadow but not the substance of true health legislation, regulation and enforcement.

Medicine on Stamps

Robert Tait McKenzie



This distinguished Canadian-born sculptor and physician (1867-1938) received his M.D. from McGill in 1892 and an L.L.D. in 1921. A pioneer in the field of physical education in medicine and the influence of exercise on the heart, his *Reclaiming the Maimed* was used by the surgeon general of the U.S. Army for reconstruction of hospitals in 1918. He was Director of Physical Ed., U. Pa. 1904-30. His important sculptures are in the Canadian House of Commons, Canadian National Gallery, and also in London, and Washington, D.C.

Text: Dr. Joseph Kler
Stamp: Minkus Publications, Inc., New York

Sputum Cytology Aids Detection Of Lung Cancer

Continued from page 1

earlier chest films and an examination of the upper respiratory tract.

Of the 35 patients whose cancers were diagnosed by sputum cytology alone, all were shown to have squamous cell carcinoma, presumably at an early stage, the Mayo researcher said. On the other hand, about half of the lung cancers detected in initial X-ray screening were at a much more advanced stage.

"About 70% of the 35 patients whose lung cancer was detected by sputum cytology and who were treated surgically or with radiation therapy appear to have a favorable outlook," Dr. Sanderson said, stressing the preliminary nature of his findings.

Conservative Surgery

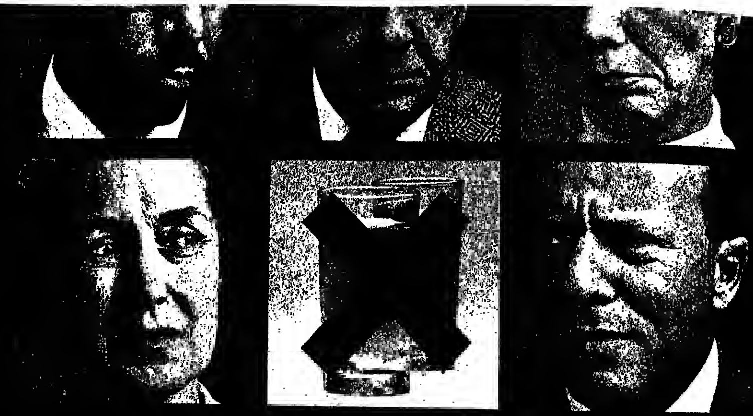
In many cases, surgery in those patients has been limited to lobectomy, Dr. Sanderson explained, noting that "our surgeons are emphasizing conservative resection to spare functional, tumor-free lung tissue. This may facilitate reoperation in some individuals who are so unfortunate as to have a subsequent second primary tumor or recurrent cancer.

"Those who haven't done as well have suffered the consequences of other smoking-related diseases, including coronary heart disease and other cardiovascular diseases, more frequently than they have had recurrences of their lung cancer."

As of late October, 9,165 male smokers over 45 have entered the Mayo Lung Project, Dr. Sanderson said. Of 7,038 men who completed the first phase of the screening program, 60 were found to have previously unsuspected cancer on entry. Among the participants who had follow-up screening examinations, 17 new cases were detected.

"Although the duration of follow-up remains brief, and the number of patients with lung cancer is relatively small, these initial data offer some encouragement ... [Through screening] persons with presymptomatic lung cancer can be identified, the tumors localized, and the patients treated ... Early results suggest long-term survival and possible improvement in the quality of life" said Dr. Sanderson, who is Associate Director of the Mayo Lung Project.

PATIENT EDUCATION can begin in your waiting room if you'll remove the special section from this paper titled **THE GOOD DRUGS DO** and put it in your waiting room. Edited by the top pharmacologist, Dr. Louis Lasagna, it will help build doctor-patient relationships. **It begins on Page 9.**



The problem of hypokalemia had a distasteful solution...

until now

matrix with a mission

...for the treatment of hypokalemia
...for the prevention of hypokalemia when dietary intake of K is inadequate

Slow-K®

(potassium chloride) slow-release tablets 8 mEq

The mission: to deliver K patients can take

The Slow-K wax matrix is ...nded to provide a controlled ...se of potassium to minimize ... likelihood of high local con...trations of potassium within the ...intestinal tract.

Comparison studies[1-3] show ...-K to be far more palatable and ...venient than liquid KCl. Fur..., Slow-K caused much less ..., heartburn and diarrhea ... of abdominal cramp... was comparable). Also, no evi...ce of GI bleeding was detected ...en Slow-K was administered ... for 14 days to 30 male volun...[4]

The mission: to deliver K patients will take

The problem of patient compliance posed by the unpleasant taste and aftertaste of liquid potassium supplements is not a factor one need be concerned with when prescribing sugar-coated Slow-K tablets. For when compared to liquid KCl preparations[1-3] or to a potassium gluconate elixir,[1,5] Slow-K proved far more palatable—as well as more convenient and more acceptable—to the great majority of patients.

The chloride anion

Slow-K provides the chloride anion which, combined with K^+, is essential for restoring normal acid-base and potassium balance in patients with hypokalemic alkalosis.[6]

Dependable potassium supplementation

Slow-K maintained normal serum K levels as effectively as liquid KCl preparations[2,3] and as a potassium gluconate elixir,[5] according to open-label crossover studies.[2,3,5]

And Slow-K has over 10 years' worldwide clinical experience, with over 4 billion tablets dispensed.*

*Potassium chloride tablets have produced stenotic and/or ulcerative lesions of the small bowel and deaths. Similar lesions have also been reported with liquid K supplements. A few cases associated with wax-matrix tablets have also been reported. The frequency of these lesions, however, is much less with wax-matrix tablets (less than 1 per 100,000 patient-years) than with enteric-coated KCl tablets (40-50 per 100,000 patient-years). Note: Solid forms of K supplements are contraindicated in any patient in whom there is cause for arrest or delay in tablet passage through the GI tract.

CONTRAINDICATIONS
In patients with hyperkalemia, since a further increase in serum potassium concentration in such patients can produce cardiac arrest. Hyperkalemia may complicate any of the following conditions: chronic renal failure, systemic acidosis such as diabetic acidosis, acute dehydration, extensive tissue breakdown as in severe burns, adrenal insufficiency, or the administration of a potassium-sparing diuretic (eg, spironolactone, triamterene).

Wax-matrix potassium chloride preparations have produced esophageal ulceration in certain cardiac patients with esophageal compression due to enlarged left atrium.

All solid dosage forms of potassium supplements are contraindicated in any patient in whom there is cause for arrest or delay in tablet passage through the G.I. tract. In these instances, potassium supplementation should be with a liquid preparation.

WARNINGS
In patients with impaired mechanisms for excreting potassium, administration of potassium salts can produce hyperkalemia and cardiac arrest. This occurs most commonly in patients given potassium intravenously but may also occur when given orally. Potentially fatal hyperkalemia can develop rapidly and be asymptomatic. Use of potassium salts in patients with chronic renal disease, or any other condition which impairs potassium excretion, requires particularly careful monitoring of the serum potassium concentration and appropriate dosage adjustment.

Hypokalemia should not be treated by the concomitant administration of potassium salts and a potassium-sparing diuretic (eg, spironolactone or triamterene), since the simultaneous administration of these agents can produce severe hyperkalemia.

Potassium chloride tablets have produced stenotic and/or ulcerative lesions of the small bowel and deaths. These lesions are caused by a high localized concentration of potassium ion in the region of a rapidly dissolving tablet, which injures the bowel wall and thereby produces obstruction, hemorrhage, or perforation. Slow-K is a wax-matrix tablet formulated to provide a controlled rate of release of potassium chloride and thus to minimize the possibility of a high local concentration of potassium ion near the bowel wall. While the reported frequency of small bowel lesions is much less with wax-matrix tablets (less than one per 100,000 patient-years) than with enteric-coated potassium chloride tablets (40-50 per 100,000 patient-years), a few cases associated with wax-matrix tablets have been reported. These data are from foreign marketing experience. Slow-K should be discontinued immediately and the possibility of bowel obstruction or perforation considered if severe vomiting, abdominal pain, distention, or gastrointestinal bleeding occurs.

Hypokalemia in patients with metabolic *acidosis* should be treated with an alkalinizing potassium salt such as potassium bicarbonate, potassium citrate, or potassium acetate.

PRECAUTIONS
Potassium depletion is ordinarily diagnosed by demonstrating hypokalemia in a patient with a clinical history suggesting some cause for potassium depletion. In interpreting the serum potassium level, the physician should bear in mind that acute alkalosis *per se* can produce hypokalemia in the *absence* of a deficit in total body potassium, while acute acidosis per se can increase the serum potassium concentration into the normal range even in the presence of a reduced total body potassium. The treatment of potassium depletion, particularly in presence of cardiac disease, renal disease, or acidosis, requires careful attention to acid-base balance and appropriate monitoring of serum electrolytes, electrocardiogram, and clinical status of patient.

ADVERSE REACTIONS
Most common to oral potassium salts: nausea, vomiting, abdominal discomfort, and diarrhea. These symptoms are due to irritation of the gastrointestinal tract and are best managed by diluting the preparation further, taking the dose with meals, or reducing the dose.

Most severe adverse effects: hyperkalemia and gastrointestinal obstruction, bleeding, or perforation.

DOSAGE AND ADMINISTRATION
Usual dietary intake of potassium by the average adult is 40 to 80 mEq per day. Potassium depletion sufficient to cause hypokalemia usually requires loss of 200 or more mEq of potassium from the total body store.

Dosage must be adjusted to the individual needs of each patient but is typically in the range of 20 mEq per day for prevention of hypokalemia to 40-100 mEq per day or more for treatment of potassium depletion.

HOW SUPPLIED
Tablets (pale orange, sugar-coated), each containing 600 mg (8 mEq) potassium chloride; bottles of 100 and 1000.

Consult complete literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

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